

REMARKS

Claims 1-25 are pending. Claim 1 and claim 8 have been amended. The amendment to claim 1 is supported in the specification at, e.g. page 6, lines 28-31 and page 10, line 31 to page 11, line 22 (Example 1). Support for the amendment to claim 8 can be found, for example, on page 10, line 22 and page 13, line 6 of the specification. Support for the amendments to the specification can also be found, for example, on page 10, line 22 and page 13, line 6 of the instant specification.. No new matter is added.

Applicants request that the Examiner in the next Communication in this case return an initialed Form-1449 corresponding to the Information Disclosure Statement submitted June 6, 2002. A supplemental information Disclosure Statement accompanies this response.

The Examiner has objected to the specification, on page 2, paragraph 1 of the Office Action, for not capitalizing the trademark "TWEEN" and accompanying it with the generic terminology. Applicants have amended the specification to capitalize TWEEN where it appears and supply the generic terminology which is "polysorbate". Support for "polysorbate-20" and "polysorbate-80" can be found, for example on page 10, line 22 and page 13, line 6 of the specification. Thus, no new matter is added with these amendments. Applicants submit that the use of TWEEN as presently amended in the specification satisfies the requirements for use of trademarks in a patent application.

Rejections under 35 U.S.C. §112, second paragraph

The Examiner has rejected claim 8, on page 2, paragraph 4 of the Office Action, for being indefinite for reciting "TWEEN-20". Applicants have amended claim 8 to replace "TWEEN-20" with "polysorbate-20".

Applicants request that this rejection be withdrawn.

Rejection under 35 U.S.C. §103

The Examiner has rejected claims 1-25, on page 3, paragraph 7, of the Office Action as obvious over Bennett *et al.* U.S. Patent No. 5,371,193 (“Bennett”) in light of Keith *et al.*, U.S. Patent No. 5,679,339 (“Keith”) and Schaefer *et al.* U.S. Patent No. 6,096,873 (“Schaefer”). The rejection is traversed to the extent it is applied to the claims as amended.

Amended claim 1, from which the remaining claims subject to the rejection depend, is drawn to IL-11 in a composition including glycine and a cryoprotectant that collectively allow the IL-11 to have reduced aggregation following storage for 26 weeks at 40° C as compared to IL-11 stored for 26 weeks at 40° C in a composition with glycine and without the cryoprotectant.

A *prima facie* case of obviousness requires some suggestion or motivation, either in the references themselves or in the knowledge generally available in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See also MPEP 706.02(j). The cited references however, alone or in combination, fail to make *prima facie* obvious the claimed composition. There is no suggestion in the Bennett, Keith, or Schaefer that combining IL-11 with glycine and a cryoprotectant would result in any added benefit, much less result in a composition characterized by reduced aggregation following prolonged storage, as required by the claims. Nor is there a reasonable expectation of success in making a composition with the required properties would be successful.

Bennett is cited for describing pharmaceutical compositions that include IL-11. Not only does Bennett fail to disclose any composition having the claimed properties, Bennett is silent on the remaining components of the claimed combination. The Examiner states that Keith discloses

compositions that include IL-11 and sucrose (a cryoprotectant), and compositions that include IL-11 and glycine. This reference, however, lacks any suggestion for making a composition that includes all of IL-11, sucrose, and glycine. The reference also lacks any suggestion that such a composition would have reduced aggregation properties.

Schaefer fails to overcome the deficiencies of Bennett and Keith. Schaefer does not disclose IL-11 but is cited instead for describing pharmaceutical formulations of gamma-heregulin that include low molecular weight proteins less than 10 amino acids, cryoprotectants, and surfactants. Applicants respectfully disagree with the Examiner's assertion that the artisan would substitute IL-11 for gamma-heregulin in Schaefer's pharmaceutical compositions. The amino acid sequences of IL-11 and gamma-heregulin, which is nearly four times larger than IL-11, show no significant homology.¹ Accordingly, one of ordinary skill in the art would not presume that these two proteins would interact similarly with the components listed above and therefore, would not be motivated to modify the teachings in Schaefer to arrive to the claimed invention.

To further illustrate this point, the instant specification teaches that IL-11 tends to form soluble high molecular weight aggregates which interferes with product quality and effectiveness. There is no teaching in Schaefer, however, that gamma-heregulin has the same technical problems. Thus, Applicants submit that one of ordinary skill in the art would not expect that replacing gamma-heregulin in the formulations of Schaefer with IL-11 as described in Bennett or Keith would be successful.

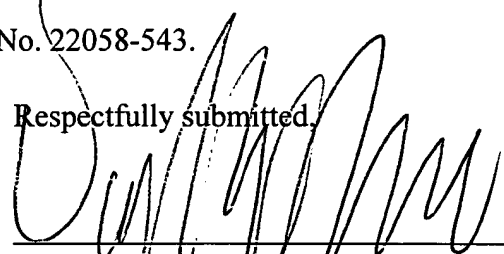
On the basis of the foregoing amendment and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding this

¹ See Exhibit A, which is a comparison of the primary amino acid structure of IL-11 and gamma-heregulin.

amendment and/or these remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

A petition for extension of time and supplemental information disclosure statement accompany this response, along with the corresponding fees. The Commissioner is authorized to charge any additional fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311, Reference No. 22058-543.

Respectfully submitted,



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TRA 1992121v3



Blast 2 Sequences results

[PubMed](#)[Entrez](#)[BLAST](#)[OMIM](#)[Taxonomy](#)[Structure](#)

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.10 [Oct-19-2004]

Matrix  gap open: gap extension:
x_dropoff: expect: wordsize: [Filter](#) ☒ 

Sequence 1 [gi 2406644](#) gamma-hereregulin [Homo sapiens] **Length** 768

Sequence 2 [gi 27501936](#) interleukin 11 [Homo sapiens] **Length** 199

No significant similarity was found

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